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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,013	11/16/2001	Shui-on Leung	IMMU:014US2	7681

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/988,013	Applicant(s) LEUNG ET AL.	
	Examiner David J. Blanchard	Art Unit 1643	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 31 December 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3 + 1* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *31 December 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *28-29 and 31-32*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 5. Applicant's reply has overcome the following rejection(s):
The rejection of claims 30 and 38-43 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the cancellation of the claims.

The rejection of claims 30 and 38-43 under 35 U.S.C. 102(b) as being anticipated by Leung et al [a] (US Patent 5,789,554, issued 8/4/1998, IDS reference A2 filed 4/30/2002) is withdrawn in view of the cancellation of the claims.

The rejection of claims 30 and 38-39 under 35 U.S.C. 102(b) as being anticipated by Leung et al [b] (Molecular immunology, 32(17-18):1413-1427, 1995, cited on PTO-892 mailed 2/20/2004) is withdrawn in view of the cancellation of the claims.

Continuation of 11. does NOT place the application in condition for allowance because:
The objection to the oath/declaration as being defective because the present application is a continuation-in-part based on the lack of adequate written description is maintained (see written description rejection immediately below).

The rejection of claims 28-29 and 31-32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained.
The reply filed 12/31/2007 states that claim 28 has been amended to incorporate the limitations of claims 30, 38 and 39, so that it now specifies that the heavy chain FR4 is selected from the human NEWM antibody, the light chain framework regions are selected from the human REI antibody, and the heavy chain FR1, FR2 and FR3 are selected from the human REI antibody, and the heavy chain FR1, FR2 and FR3 are selected from the human EU antibody. Applicant notes that these are selections used in the humanized LL2 antibody that is described in the present application, and therefore the proposed amendment addresses certain concerns raised in the interview summary mailed 8/8/2007. Applicant states that the same human framework selections were used to produce other humanized antibodies, demonstrating that the presently claimed selections are useful to produce a genus of humanized antibodies that differ in their specificities. Applicants' arguments have been fully considered but are not found persuasive for at least the reasons already of record. As an initial matter, it is noted that dependent claims 30 and 38-39 were also included in the instant rejection and thus, it is unclear to the examiner how applicants' incorporation of the dependent limitations into base calim 28 overcome the instant rejection. The issue remains that there is a lack of adequate written description for the method of producing the subgenus of humanized antibodies comprising just any CDRs in the context of human REI light chain farmeworks and the human heavy chain EU FR1-3 regions and the human NEWM FR4 region. As noted by applicant, the written description only sets forth a single species, wherein murine monoclonal antibody LL2 was humanized according to the claimed method in which the LL2 CDRs of the light chain were grafted onto human REI frameworks and the heavy chain CDRs were grafted onto the human EU frameworks, except for FR4, which was from the human NEWM antibody and wherein the most homologous human framework sequences were selected. The instant claims do not recite the LL2 CDRs and encompass any CDRs in the context of the specificed frameworks, whereas the written description sets forth that human frameworks exhibiting the highest sequence homology should be selected and murine framework residues which might affect affinity and specificty of the humanized antibody were retained in the design of the humanized framework sequences. The specification does not fully develop the concept that there are universal or best fit human frameworks for humanization in which just any non-human CDRs may be grafted and retain the antigen specificty and affinity of the parental non-human antibody. Further, in light of the prior art, e.g., Gorman et al, such a universal property appears to be unpredictable since different antibodies will have different amino acids in the framework which are important for antigen binding and stability, consistent with the written description of the present application. Applicant's reliance on a single disclosed species is insufficient to support the broader scope of the claims encompassing multiple subgenera because there is insufficient disclosure of a "representative number of species" and there is substantial variation and unpredictability within the subgenera claimed. One of skill in the art would not recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the subgenus of the claimed method in view of the single disclosed species.
Applicants' arguments with respect to other antibodies produced by the presently claimed human farmework selections is not found persuaisve because the issue is not whether one of skill could make and use the claimed method, which goes more towards enablement, but rather whether the written description necessarily discloses the claimed subject matter. Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000) at page 1486 states "It is 'not a question of whether one skilled in the art might be able to construct the patentee's device from the teachings of the disclosure. ... Rather, it is a question whether the application necessarily discloses that particular device.'") (quoting Jepson v. Coleman, 314 F.2d 533, 536, 136 USPQ 647, 649-50 (CCPA 1963))
Applicant is again reminded that the written description requirement is separate and distinct from the enablement requirement. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991). An invention may be enabled even though it has not been described. See, e.g., In re DiLeone, 436 F.2d 1404, 1405, 168 USPQ 592 (CCPA 1971) ("[I]t is possible for a specification to enable the practice of an invention as broadly as it is claimed, and still not describe that invention.").
For these reasons and those already of record, the rejection is maintained.

The disclosure of the prior-filed application, USSN 08/820,576 with which applicant argues, does not to provide adequate support in the manner provided by the first paragraph of 35 U.S.C. 112 for the present claims (see immediately above).
The later-filed application must be an application for a patent for an invention, which is also disclosed, in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The rejection of claims 28-29 and 31-32 under 35 U.S.C. 102(b) as being anticipated by Leung et al [a] (US Patent 5,789,554, issued 8/4/1998, IDS reference A2 filed 4/30/2002) is maintained.
The response filed 12/31/2007 states that the instant application is a continuation of USSN 09/741,843, filed 12/22/00, which was a continuation of USSN 09/127,902, filed 8/3/98 (now U.S. Patent No. 6,187,287), which was a continuation of USSN 08/690,102, filed

7/31/96 (now U.S. Patent No. 5,789,554), which was a continuation of USSN 08/289,576, filed 8/12/94. Support for the instant claimed subject matter may be found going back to the original priority document, USSN 08/280,576, filed 8/12/94, and as detailed in applicants' previous responses, this reference is not effective as priro art. Applicants' arguments have been fully considered but are not found persuasive. The disclosure of the prior-filed application, USSN 08/820,576 with which applicant argues, does not to provide adequate support in the manner provided by the first paragraph of 35 U.S.C. 112 for the presently claimed subject matter as discussed supra (see written description rejection above).

The rejection of claims 28-29 and 31-32 under 35 U.S.C. 102(b) as being anticipated by Leung et al [b] (Molecular immunology, 32(17-18):1413-1427, 1995, cited on PTO-892 mailed 2/20/2004) is maintained.
Applicant argues as above against Leung et al [a] and the examiners' remarks above apply here as well and as such the rejection of claims 28-29 and 31-32 under 35 U.S.C. 102(b) as being anticipated by Leung et al [b] is maintained.

Respectively,
/David J. Blanchard/
571-272-0827